REMARKS

Claims 1, 10-11, 15 and 29-30 are pending in the application. Claims 2, 3, 5 and 7 have been cancelled. All non-elected claims have also been cancelled without prejudice. New claims 29 and 30 have been added to claim the treatment of T cells in vitro. The addition of these claims would not require a new search because the applicants have only removed the step of administering treated T cells back into the patient. The prior search of the former claims necessarily already required the search of these new claims. Applicants reserve the right to re-file non-elected claims in a divisional application.

Information Disclosure Statement:

The information disclosure statement transmittal had the box checked under 37 CFR 1.97(b) indicating that it had been mailed before the mailing of the first Office Action on the merits. The first Office Action on the merits was mailed on January 17, 2006. The information disclosure statement was mailed on September 23, 2004.

Further, the information disclosure statement was mailed within 3 months of the mailing of the international search report. For a complete record, the Applicant submits a statement under 37 CFR 1.97(e).

Priority:

The priority of the present utility application is supported by the documents that were filed as part of the provisional application. The abstract of the Journal of Immunology article (2002) indicates that the "approach can be used therapeutically in conditions where increased production of IL-2 is desired."

It is submitted that the applicants had possession of the invention, i.e. the treatment of humans with T cells that have been gene modified. The treating of humans with gene modified T cells would be expected by one of ordinary skill in the art to work in practice because the Applicants have shown how to treat the T cells in vitro, that the treated T cells remained viable, and the desired result of removing the defect that causes the symptoms of lupus was achieved in vitro in the T cells. It is also known to remove T cells and introduce them back into the same person in the medical field. Therefore, priority is supported by the prior priority application.

The claims 1-3, 5 and 15 have been rejected under 35 USC 112, second paragraph. Claims 1, 5, 7 and 28 have been objected to.

Amendments to claims 1, 10, 11 and 15 have been made to address the Examiner's comments. Claims 7 and 28 have been cancelled. It is respectfully submitted that the rejection and objections are now overcome.

Claims 1-3, 5, 10-11 and 15 have been rejected under 35 USC 112, first paragraph as allegedly not enabled. Applicants respectfully traverse this rejection.

The Applicants have laid the ground work for the method of the invention in terms that are understood by one of ordinary skill in the art. On page 11, it states:

"The cAMP response element modulator (CREM) has been shown by the inventors to bind specifically to the -180-site of the interleukin-2 promoter in vitro. CREM protein was found increased in T cells of patients with systemic lupus erythematosus (SLE), and it is considered responsible for the decreased production of IL-2. The inventors have found that transcriptional upregulation is responsible for the increased CREM protein levels and that CREM binds to the IL-2 promoter in live SLE T cells. The inventors have found that suppression of the expression

of CREM mRNA and protein by an anti-sense CREM plasmid, which was forced to express in SLE T cells by electroporation, resulted in decreased CREM protein binding to the IL-2 promoter and increased expression of IL-2 mRNA. The inventors have found that anti-sense constructs can be used to effectively eliminate the expression of a transcriptional repressor. This approach can be used therapeutically in conditions where increased production of IL-2 is desired for the treatment of SLE."

On page 13, it states:

"..we demonstrate that an anti-sense CREM plasmid not only decreases the expression of CREM mRNA and protein, but also upregulates the defective expression of IL-2 in SLE T cells."

On page 38, it states:

"Treatment of humans: We propose to leukophorese patients (remove lymhocytes with an apparatus widely used to collect pleatelets in blood banks, subject them to electroporation, whereby we will insert, a zeta chain construct and then reinfuse the cells into the patient. Similar approach will be used for the insertion of the antisense CREM.

The sequences for TCR chain, C terminal TCR ζ chain mAb, TCR/CD3 complex, P65 subunit of the nuclear factor-κB, NF-κB, IL-2, Fc receptor γ chain, and CREM are all known and deposited in the NCBI (NIH) data base.

There are several types of apparatuses on the market for removing T cells from a patient and they are routinely used by blood banks. The blood will come out from one arm vein, will be centrifuged (it is a closed system) and the lymphocytes will be removed. They will be transfected with the appropriate vector and then, they will be re-administered through an arm vein. The leukapheresis apparatus delivers T cells back into the body as well as remove them. Transfection of cells will take place under sterile conditions.

The dose range will be between 10 million cells and build up to 1 billion."

These passages show that the inventors had possession of the invention, i.e. the treatment of humans with T cells that have been gene modified. The inventors submit that the invention of treating humans with gene modified T cells would be expected by one of ordinary skill in the art to work in practice based on the in vitro data. This is because the inventors have show how to treat the T cells in vitro, that the treated T cells remained viable, and the desired result of removing the defect that causes the symptoms of lupus was achieved in vitro in the T cells. (see figures 3, 4A and 4B, 5A, 5B, 6)

It is also submitted that the step of returning the gene modified T cells back into the patient is supported by the specification because the dose and method of transfer have been presented. It is known in the art to remove T cells from patients with other illnesses, treat them, and then return them to patients. Therefore, it is reasonable to believe that the return of the gene modified T cells of the invention that show the desired effects in vitro to the patient, would inherently work in vivo. Returning T cells that are functioning normally would not be regarded to be dangerous or be expected to fail the intended purpose of treating SLE.

The step of electroporation of the T cells occurs outside of the body. It is not attempted inside the body. After electroporation, the T cells at issue were found viable, functioning like normal T cells and having the wrongly expressed genes corrected. Therefore, the applicants submit that one of ordinary skill in the art would not expect that the step of electroporation of the T cells would make them unacceptable for reintroduction into the body.

Regarding the issue of the absence of the gene sequence for CREM or antisense CREM in the specification, it is submitted that these sequences are well known and

available in the literature and therefore, are not required to be recited for enablement. For instance, the following publications are presented for the sole purpose of showing that such publications reciting the sequence at issue do exist:

1. Foulkes, N. S., Borrelli, E., and Sassone-Corsi, P. 1991. CREM gene: use of alternative DNA-binding domains generates multiple antagonists of cAMP-induced transcription
282. *Cell* 64:739-749.

2. Molina, C. A., Foulkes, N. S., Lalli, E., and Sassone-Corsi, P. 1993. Inducibility and negative autoregulation of CREM: an alternative promoter directs the expression of ICER, an early response repressor
. *Cell* 75:875-886.

3. Foulkes, N. S., Mellstrom, B., Benusiglio, E., and Sassone-Corsi, P. 1992. Developmental switch of CREM function during spermatogenesis: from antagonist to activator
Nature 355:80-84.

Reconsideration and allowance are respectfully requested.

Respectfully submitted,

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